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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,537	08/04/2003	Kyriacos C. Nicolaou	TSRI 904.1	6050

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EXAMINER

STOCKTON, LAURA LYNNE

ART UNIT PAPER NUMBER

1626

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/634,537	<b>Applicant(s)</b> NICOLAOU ET AL.	
	<b>Examiner</b> Laura L. Stockton, Ph.D.	<b>Art Unit</b> 1626	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 January 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3,9,11-13,15-18,27 and 29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 15-18 and 29 is/are allowed.
- 6) ☒ Claim(s) 1-3, 9, 11-13 and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

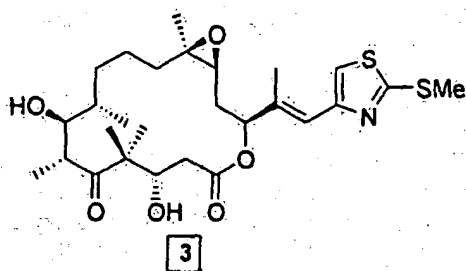
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## DETAILED ACTION

Claims 1-3, 9, 11-13, 15-18, 27 and 29 are pending in the application.

### *Election/Restrictions*

Applicants' election without traverse of Group I, and the species of claim 14 which corresponds to compound 3 of Figure 1A (reproduced below), in the reply filed on May 20, 2005 is acknowledged.



Applicants cancelled claims 4-8, 10 and 19-26 as being directed to non-elected subject matter.

Rejections made in the previous Office Action that do not appear below have been overcome. Therefore,

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arguments pertaining to these rejections will not be addressed.

***Terminal Disclaimer***

The three terminal disclaimers filed on January 12, 2006 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Pat. 6,531,497, and any patent resulting from 10/732,698 and 10/227,073, have been reviewed and are accepted. All three terminal disclaimers have been recorded.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

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said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 9, 11-14 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vite et al. {WO 99/54318}, Nicolaou et al. {WO 99/67252} and Klimko {WO 2003/026744}, each taken alone or in combination with each other.

***Determination of the scope and content of the prior art (MPEP §2141.01)***

Applicants claim analogs of epothilone. Vite et al. (pages 1, 2 and 7-10; and especially Example 1 on page 16), Nicolaou et al. (pages 2-4, 21, 26, 29 and 30; and especially the compound of Example 6(ix) on page 58) and Klimko (formula I, pages 4-8 and 11-13; and especially Compound 2 on page 7) each teach analogs of epothilone which are either structurally the same as (see above 102 rejection) or structurally similar to the instant claimed compounds.

***Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)***

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The difference between some of the compounds of the prior art and the compounds instantly claimed is that the instant claimed compounds are generically described in the prior art.

*Finding of prima facie obviousness--rational and motivation (MPEP  
§2142-2413)*

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., cytotoxic agents).

One skilled in the art would thus be motivated to prepare compounds embraced by the prior art to arrive at the instant claimed compounds with the expectation of obtaining additional beneficial compounds which would be useful as a cytotoxic agent. Since each of the prior art references teach analogs of epothilone which are structurally similar to each other, the

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combination of the prior art references would also teach the instant claimed invention. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art. A strong case of *prima facie* obviousness has been established.

### ***Response to Arguments***

Applicants' arguments filed January 12, 2006 have been fully considered but they are not persuasive. Applicants argue that: (1) Vite et al. disclose a synthetic procedure of producing their epothilones and one skilled in the art could not make the instantly claimed compounds using the methodology disclosed in Vite et al.; (2) Nicolaou et al. do not disclose or suggest the advantageous activity of Example 6(ix), which corresponds to instant compound 3 (formally found in cancelled claim 14); (3) Klimko do not disclose any other epothilones other than those taught by Vite et al. and Nicolaou et al.

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All of Applicants' arguments have been considered but have not been found persuasive. On pages 11 and 12, Vite et al. teach various processes of preparing their epothilones. Vite et al. also teach that some of the processes steps are those known in the art. Also see the processes of making in Nicolaou et al. starting at the bottom of page 22 through page 29 and in Klimko on page 7, lines 6-17 through to page 8, lines 1-19. Applicants argue that Nicolaou et al. do not disclose or suggest the advantageous activity of Example 6(ix). In response, Nicolaou et al. teach that their compounds are useful in the treatment of various cancers (see page 8, under "Bioactivity"). The Klimko reference was applied against the instant claims to show the interchangeability of the X variable representing O or CH<sub>2</sub> in pharmaceutically active compounds. For all the reasons given above, the rejection is maintained.



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The elected species of compound 3, found in Figure 1A, is not allowable over the art of record (see WO 99/67252).

### ***Allowable Subject Matter***

Claims 15-18 and 29 are allowed over the art of record.

### ***Conclusion***

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of

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this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

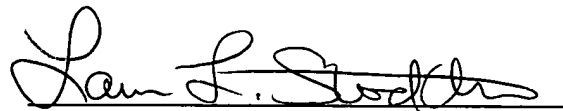
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact

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the Electronic Business Center (EBC) at 866-217-9197  
(toll-free).

The Official fax phone number for the organization  
where this application or proceeding is assigned is  
(571) 273-8300.

A handwritten signature in black ink, appearing to read "Laura L. Stockton", written over a horizontal line.

Laura L. Stockton, Ph.D.

Patent Examiner

Art Unit 1626, Group 1620

Technology Center 1600

March 22, 2006